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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,894	01/09/2002	Jinrui Shi	1286	5731

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PIONEER HI-BRED INTERNATIONAL INC.
7100 N.W. 62ND AVENUE
P.O. BOX 1000
JOHNSTON, IA 50131

EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,894	SHI ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *5,12 and 22-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-11 and 13-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/4/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-46 are pending.

2. Applicant's election with traverse of Group I, claims 1-4, 6-11 and 13-21 including SEQ ID NO:7 encoding SEQ ID NO:8 filed 3/11/2004 is acknowledged. The traversal is on the ground(s) that the MPEP states that up to ten nucleotide sequences can be claimed in a single application. Applicants also contend that the nucleotide sequences of claim 1 do not constitute independent and distinct inventions because the same primer pair was used to isolate them and the sequences have the same function. This is not found persuasive because, in regards to the permissible number of sequences as specified in the MPEP, those guidelines were for EST sequences which are much shorter than the nucleic acid sequences presented in the present application, and because of the vast number of sequences now present in the current databases that must be searched, the office does not have the resources to search more than one corresponding pair of nucleic acid and amino acid sequences per application. And lastly, according to the MPEP, up to ten sequences will be examined, and one sequence is considered up to ten, for the reasons stated above. The Office contends that the nucleotide sequences of claim 1 are sufficiently dissimilar such that a search of one sequence for prior art will not cover a search of another claimed sequence.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5, 12, and 22-46 have been withdrawn from consideration because the claims are drawn to non-elected inventions.

3. Claims 1-4, 6-11 and 13-21 are examined in the present office action.

Specification

4. It appears that Applicant has used trademarks in this application. See for example page 36, line 25, "TRIzol Reagent" and page 38, line 5, "Q-bot". It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claims 1 and 4 are objected to for reading on non-elected inventions. Correction is requested.

Claim 13 is objected to for being dependent on a non-elected claim. For purposes of compact prosecution, claim 13 will be interpreted to contain all the limitations of the claim from which it is dependent. Correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4, 6-11, 13-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid comprising a polynucleotide having at least 75% sequence identity compared to the full-length sequence of SEQ ID NO:7, a polynucleotide amplified from a plant using primers of SEQ ID NO:26 and 27 or primers determined by the software as listed in claim 1C, a polynucleotide coding for a plant inositol polyphosphate kinase (IPPK) protein other than from Arabidopsis, or a ribonucleic acid sequence encoding a protein having at least 25 contiguous amino acids of SEQ ID NO:8, or a polypeptide having at least 60% sequence identity with SEQ ID NO:8 , vector, host cell, and plant transformed therewith, and method for modulating inositol polyphosphate kinase activity in a host cell or plant comprising transforming said host cell or plant with said polynucleotide.

Applicants isolated a cDNA clone from a maize cDNA library using primers comprising SEQ ID NO:26 and 27. The isolated cDNA of SEQ ID NO:7 encodes an inositol polyphosphate kinase (IPPK) protein of SEQ ID NO:8 (pages 36-39, Examples 1-3; and sequence listing).

The Applicants do not identify essential regions of an IPPK protein encoded by SEQ ID NO:7, nor do Applicants describe any polynucleotide sequences that have at least 75% sequence identity with SEQ ID NO:7 that encode a functional IPPK protein or encode a polypeptide comprising at least 25 contiguous amino acids of SEQ ID NO:8. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical

genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a IPPK protein falling within the scope of the claimed genus of polynucleotides which have at least 75% sequence identity with SEQ ID NO:7, a ribonucleic acid sequence encoding a polypeptide comprising at least 25 contiguous amino acids of SEQ ID NO:8 or a polynucleotide that encodes any IPPK protein from any plant other than Arabidopsis. Applicants only describe a single cDNA of SEQ ID NO:7. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the IPPK protein, it remains unclear what features identify a maize IPPK protein. Since the genus of IPPK proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

7. Claims 1-4, 6-11, 13-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid comprising a polynucleotide having at least 75% sequence identity compared to the full-length sequence of SEQ ID NO:7, a polynucleotide amplified from a plant using primers of SEQ ID NO:26 and 27 or primers determined by the software as listed in claim 1C, a polynucleotide coding for a plant inositol polyphosphate kinase (IPPK) protein other than from Arabidopsis, or a ribonucleic acid sequence encoding a protein having at least 25 contiguous amino acids of SEQ ID NO:8, or a polypeptide having at least 60% sequence identity with SEQ ID NO:8 , vector, host cell, and plant transformed therewith, and method for modulating inositol polyphosphate kinase activity in a

host cell or plant and method of decreasing the level of phosphorous in non-ruminant animal waste, comprising transforming said host cell or plant with said polynucleotide.

Applicants isolated a cDNA clone from a maize cDNA library using primers comprising SEQ ID NO:26 and 27. The isolated cDNA of SEQ ID NO:7 encodes an IPPK protein of SEQ ID NO:8 (pages 36-39, Examples 1-3; and sequence listing). Applicants disclose the introduction of said cDNA sequence into immature maize embryos (pages 43-44, section B)

Applicants have not reduced to practice the claimed invention. Applicants only disclosed the cloning of SEQ ID NO:7 encoding SEQ ID NO:8, but Applicants do not disclose the outcome of transforming said sequence into maize. Applicants do not report if the introduced nucleic acid increased the phytic acid content or if inositol polyphosphate kinase activity or levels were modulated. Applicants do not teach by way of example the use of the claimed sequences to modulate IPPK activity or levels.

Applicants are claiming a series of plants overexpressing a nucleic acid sequence encoding inositol polyphosphate kinase operably linked in sense orientation with the intention of modulating the activity of said endogenous gene with an ultimate goal of reducing the phytate levels of seeds. The state-of-the-art teaches that "the biosynthetic route leading to phytate is complex and not completely understood" (Martino-Catt et al, March 6, 2001, U.S. Patent Number 6,197,561; column 2, lines 59-61). Bohnert et al (1995, The Plant Cell 7:1099-1111) teach that myo-inositol 1-phosphate is a substrate/starting material for many diverse products other than phytate (page 1102, Figure 1).

Applicants' claims are drawn to modulating IPPK activity or levels, but it is unclear how transforming a plant with a nucleic acid operably linked to a promoter in sense orientation will

both increase and decrease the activity of IPPK and subsequently reduce the level of phytate in a plant. Overexpressing SEQ ID NO:7 will increase the activity of IPPK of SEQ ID NO:8, thereby increasing the phytate level, decreasing the level of non-phytate phosphorous of a plant and increasing the level of phosphorous in non-ruminant animal waste.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that are 75% sequence identical to SEQ ID NO:7 or nucleic acids that are produced by PCR using primers of SEQ ID NO:26 and 27 will encode a protein with the same activity as a protein encoded by SEQ ID NO:7. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:7 as probes or by designing primers to undisclosed regions of SEQ ID NO:8 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify

those, if any, that when over-expressed have inositol polyphosphate activity and exhibit 75% sequence identity with SEQ ID NO:7.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 10-11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 10-11 are drawn to a seed of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only three quarters of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed seeds, it is unclear whether the claimed seeds would be distinguishable from seeds that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy , Coats, and Malik* 195 USPQ 344, (CCPA) 1977. The amendment of

the claims to recite that the seeds comprise the construct that was introduced into the parent plant would overcome the rejection.

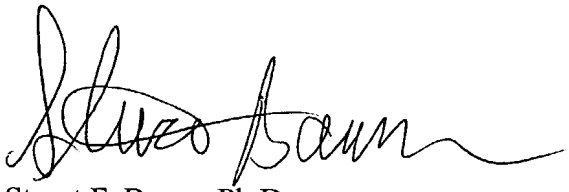
9. Claims 1-4, 6-11 and 13-21 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:7 encoding SEQ ID NO:8, and vector, host cell and plant transformed therewith and a method for modulating inositol polyphosphate kinase and method of decreasing the level of phosphorous in non-ruminant animal waste comprising said polynucleotide.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
May 27, 2004